

# Repetitive inflexible behaviors: *Measurement, mechanism, & intervention*



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Interagency Autism Coordinating Committee

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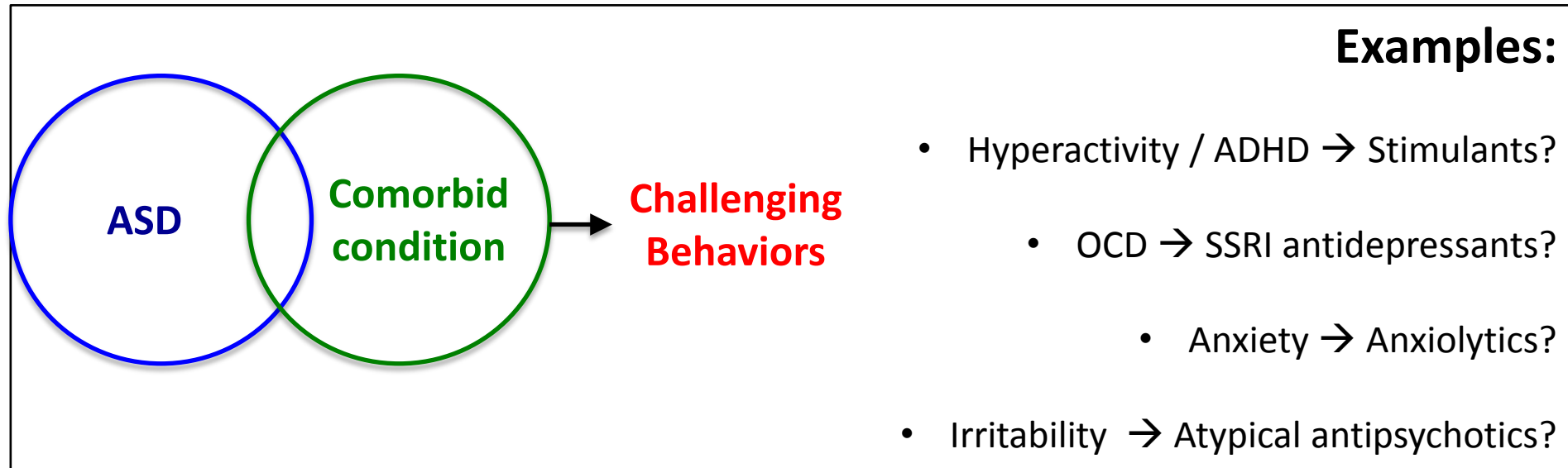
# Autism & challenging behaviors

- Many forms:
  - “Meltdowns”
  - Wandering
  - Self-injury
  - Aggression
  - Food refusal
  - Mouthing / Pica
  - Overactivity
  - etc



- Common in ASD
- Can persist into adolescence, adulthood
- Stressful for families
- Limit quality of life
- Can diminish response to other forms of intervention
- Increase cost of care

# *Comorbidity Model*

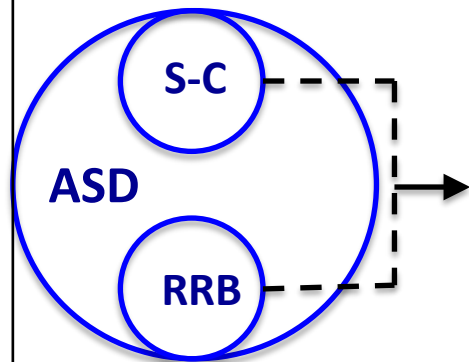


## **Limitations:**

- Diagnostic challenges
- Limited efficacy of most existing medications
- Costly
- High prevalence of drug prescriptions & polypharmacy
- Limited applicability as early intervention

# Core Features Model

## Examples:



## Challenging Behaviors

- Social isolation → anxiety / depression?
- Communication limitations → frustration / aggression?
- Lack of predictability → stress / self-injury?

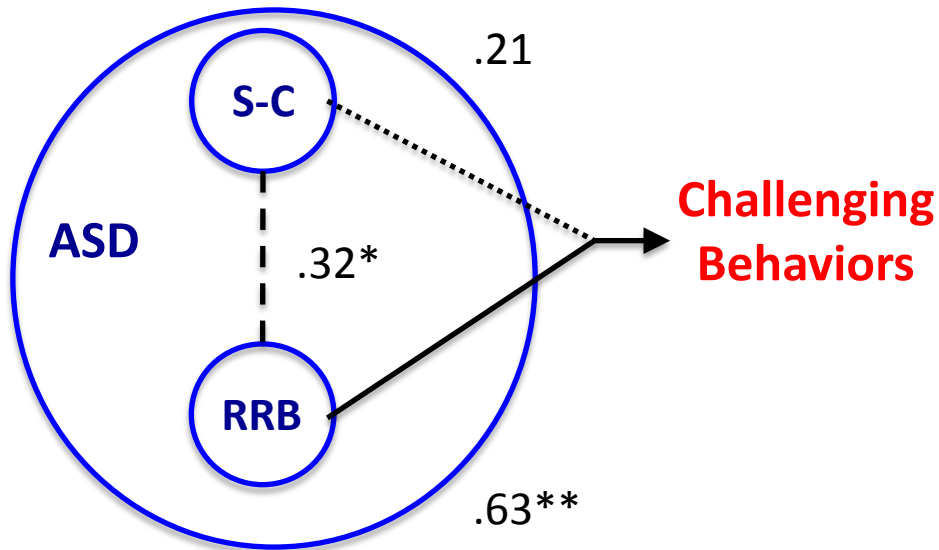
## Limitations:

- Largely untested

## Potential advantages:

- Parsimony & face validity
- Framework for novel intervention development
  - Developmental-behavioral
  - Pharmacologic
  - Early intervention

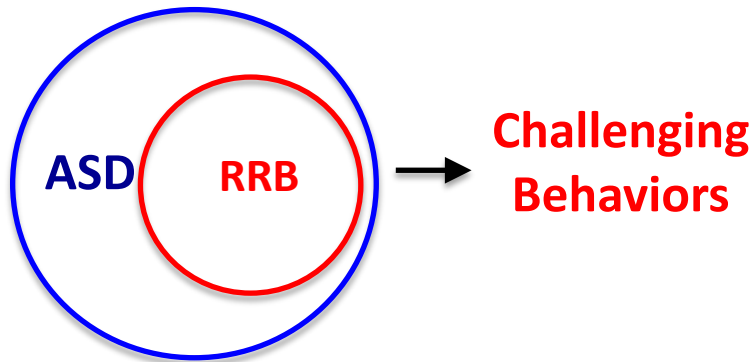
# Testing the Core Features Model



## Method:

- N = 221 ASD (ADOS, ADI)
  - 2 – 20 years
  - 61% verbal
  - 79% male
- Parent reported:
  - Social deficits (SRS)
  - Repetitive behaviors (RBSR)
  - Problem behaviors (ABC)

# Repetitive behavior & challenging behaviors



## Examples:

- When routine changes → meltdowns?
- To get access to special interest → wandering?
  - Sensory overload → self-injury?

## Approach

### *Samples (children; adult)*

- ASD: HFA, LFA
- Comparison: OCD, Depression, Social Anxiety
- Control: Typically developing

### *Methods*

- Psychometric measures
- Biomarkers

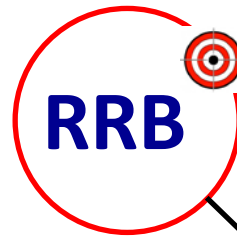
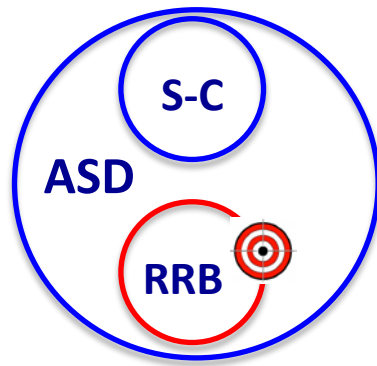
NIMH R01 Repetitive behaviors in ASD (Bodfish, Dichter)

NIMH K08 Autism & Depression (Gotham)

Autism Speaks Predoctoral Fellowship (Unruh)

NICHD R01 Behavioral Inflexibility – Outcome measurement (Boyd, Lecavalier, Bodfish)

# From targeted phenotype to targeted treatment?



- How to measure phenotype?
- What is a plausible mechanism?
- How can this phenotype be modeled pre-clinically?
- How would this inform treatment development?

Research core services:

NICHD U54 UNC IDDRC (Piven)

NICHD U54 Vanderbilt IDDRC (Dykens)

## Evidence for three subtypes of repetitive behavior in autism that differ in familiarity and association with other symptoms

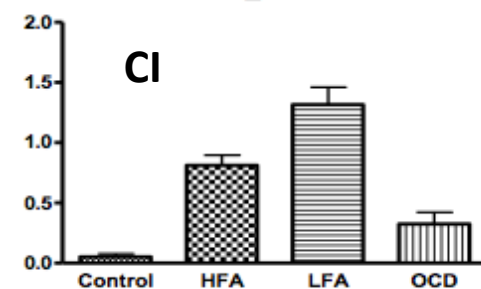
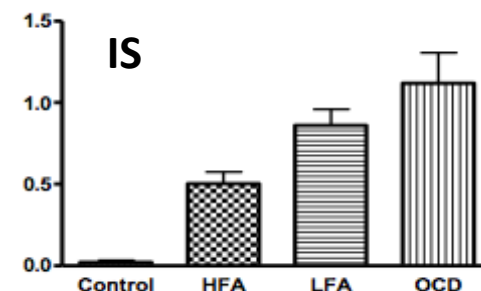
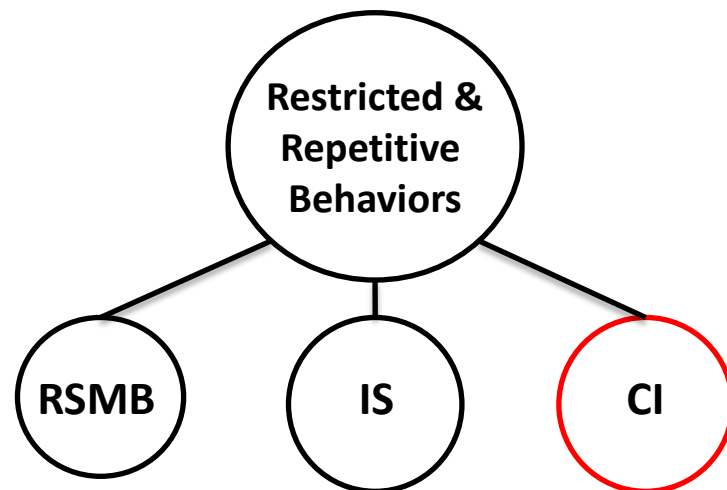
Kristen S.L. Lam,<sup>1</sup> James W. Bodfish,<sup>1,2</sup> and Joseph Piven<sup>1,2</sup>

<sup>1</sup>Neurodevelopmental Disorders Research Center, University of North Carolina – Chapel Hill, NC, USA;

<sup>2</sup>Department of Psychiatry, University of North Carolina – Chapel Hill, NC, USA

**Table 2** Results of principal components analysis and exploratory factor analysis ( $N = 316$ )

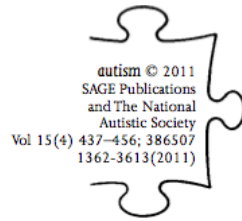
ADI-R RRB items	PCA		
	RMB	IS	CI
70 Circumscribed interests	-.39	.23	<b>.47</b>
71 Unusual preoccupations	.09	.18	<b>.67</b>
72 Repetitive use of objects	<b>.73</b>	.01	.26
73 Difficulties with minor changes in personal routine & environment	.03	<b>.75</b>	.28
74 Resistance to trivial changes in environment	.03	<b>.80</b>	-.14
75 Compulsions/rituals	-.01	<b>.67</b>	.08
76 Unusual attachments to objects	.25	-.11	<b>.60</b>
81 Hand & finger mannerisms	<b>.74</b>	.05	-.15
84 Other complex mannerisms or stereotyped body movements	<b>.77</b>	.01	.09
85 Rocking	.37	.32	-.29



- Repetitive sensory motor behavior (RSMB)
- Insistence on sameness (IS)
- Circumscribed interests (CI)
  - Unique to ASD (ASD > OCD)
  - Not associated with social impairment or IQ
  - Heritable (sib-sib correlation)
  - Common (74% of ASD)



# Phenomenology and measurement of circumscribed interests in autism spectrum disorders



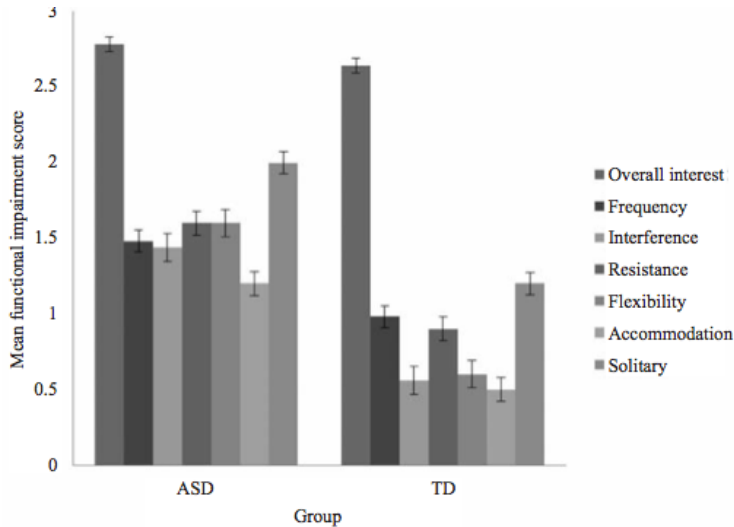
LAUREN M. TURNER-BROWN Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, USA

KRISTEN S.L. LAM Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, USA

TIA N. HOLTZCLAW Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, USA

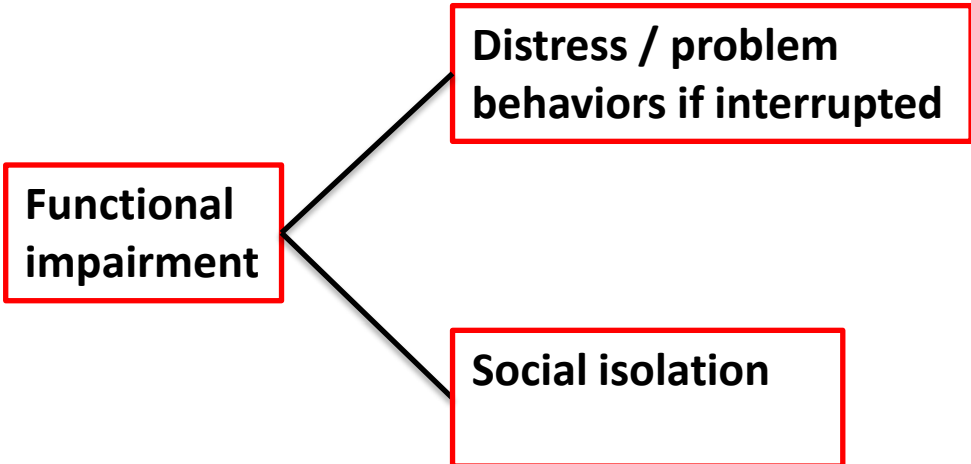
GABRIEL S. DICHTER Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, USA

JAMES W. BODFISH Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, USA



**Table 3 The Interview for Repetitive Behavior: Circumscribed Interests in the ASD sample (n = 57)**

Category	Percentage of children	Examples of circumscribed interests
Physics	56% (n = 30)	Cranes/mechanical function Preoccupied with trains Legos
Attachments	48% (n = 26)	Carries a piece of cloth with him everywhere Attached to stuffed dog Jewelry – upset when taken off
Taxonomy (primarily collecting)	33% (n = 18)	Pokemon card collecting Interest in dinosaurs – collects them Collects rocks
Television	30% (n = 16)	Cartoon network Star Wars movies Sponge Bob
Biology	17% (n = 9)	Birds of prey Evolution/dinosaurs Cougars
Facts	13% (n = 7)	Prints Wikipedia articles about videogame characters Details about actors/directors of movies Confederate wars
Mathematics	11% (n = 6)	N. 22 is his number; 22nd day of month is his day Interest in dates. Numbers – clocks, calendars, exit numbers Reads math theory books
Sensory	8% (n = 4)	Stares at anything in motion Fascination with running water for hours Watches washing machine spin



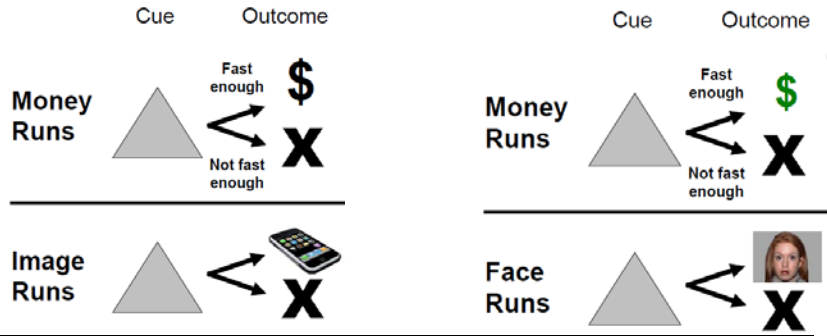
# The family perspective:

- **“Parents report that preoccupations, and intense unusual interests are among the most difficult symptoms of autism to deal with on a day-to-day basis.”**

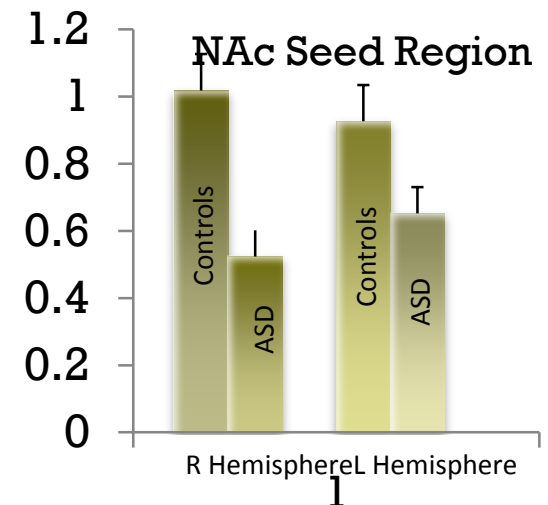
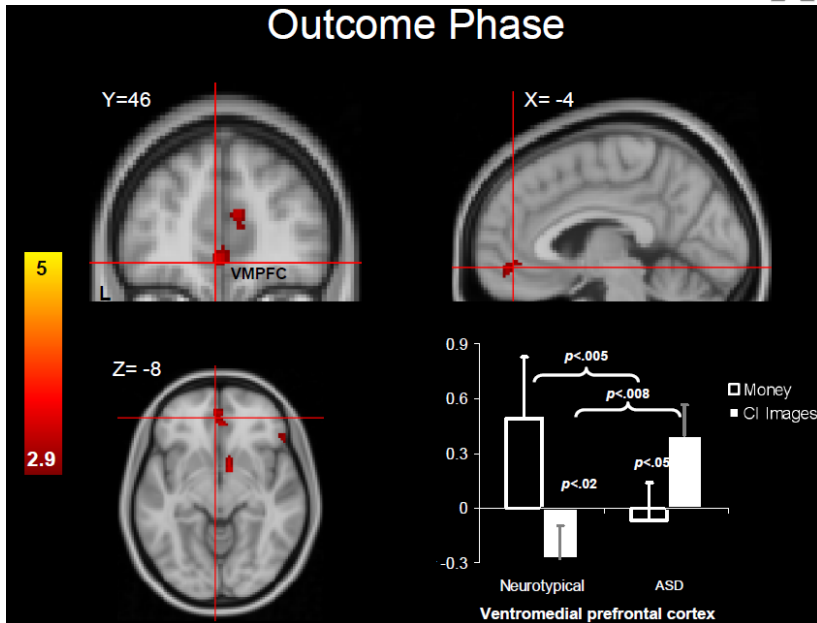
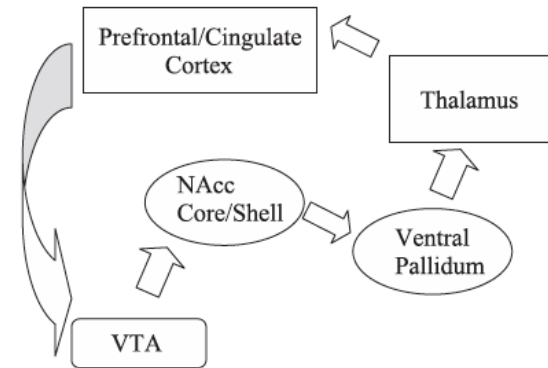
(South, Ozonoff, & McMahon, 2005)

# Mechanism? Social & Nonsocial Reward in ASD

## fMRI – Incentive Delay Paradigm



## Functional connectivity of reward circuitry



Increased BOLD signal to nonsocial rewards + Decreased frontal → striatal connectivity

# An addiction-like model of circumscribed interests & challenging behavior in ASD

- Addictions (substances, activities) evolve by “co-opting” adaptive reward processes; enhanced experience of reward (pleasure) leads to ever-growing anticipation of the experience and inability of consumption to meet anticipated outcome.
- Application to ASD?
  - Nonsocial interests develop early and increase in intensity with age
  - Intense interest narrows range of potential other experiences (including social experience)
  - “Motivational toxicity” – as idiosyncratic interest grows, interests in other areas may diminish
  - Mood and behavior problems may evolve as a reactions to interrupting intense interest (which can further restrict experiences).

# Biomarker? Social & nonsocial visual exploration



- “Visual Exploration Task” (VET)
- Passive task
- 12 static arrays
  - Faces + Objects
- 10 seconds / array
- Feasible for infants / toddlers, minimally verbal

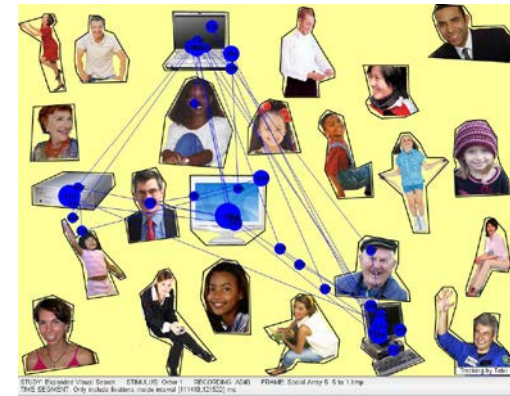
**TYP example trial**

**ASD example trial**

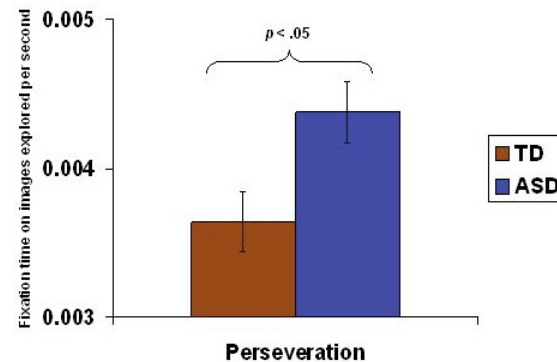
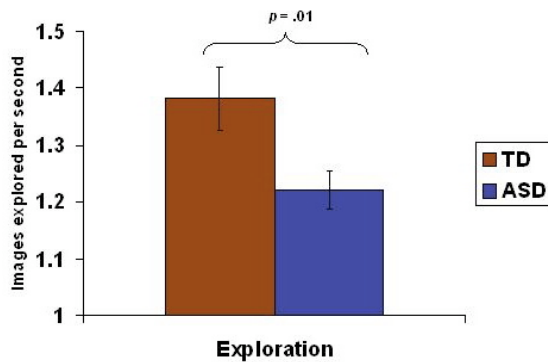
TYP



ASD



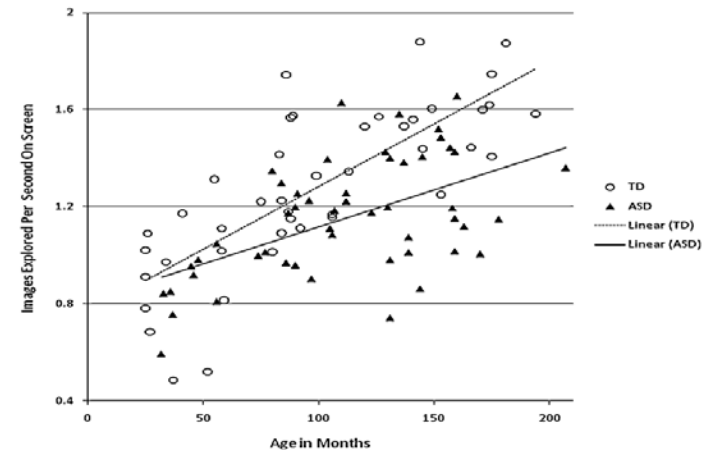
### ASD explored fewer social images & perseverated more on nonsocial images:



### Nonsocial bias increases with age in ASD:

*Sasson et al., Autism Research 2008*

*Elison et al., JADD 2012*

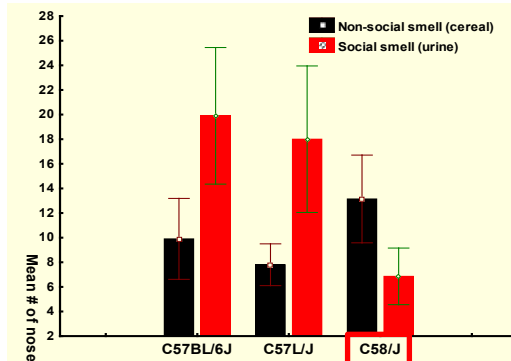
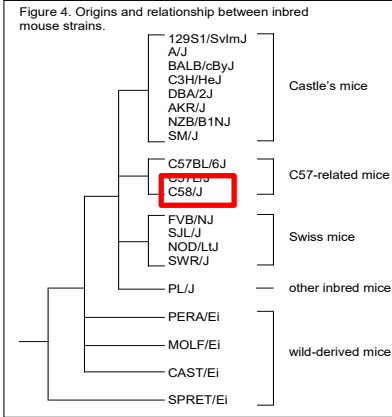


# Preclinical model? Exploration / foraging is conserved across species

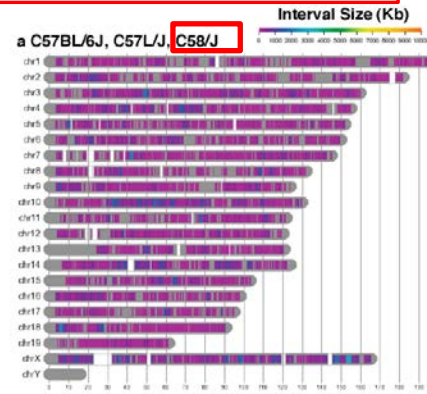
## A. Behavioral assay



## B. Screen ASD mouse models

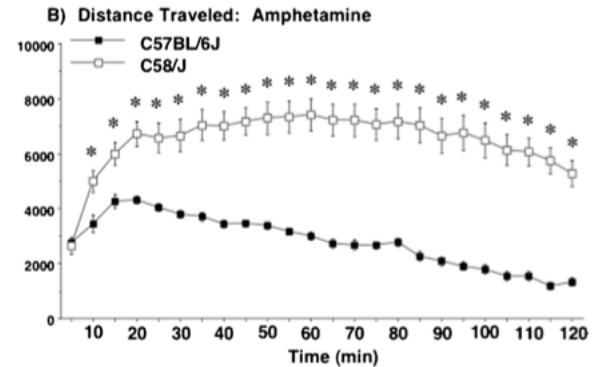


## C. Genetic analysis



- CACNA1C
- CNTNAP2
- DISC1
- NRG2
- TPH2
- GABRA5
- GABRB1
- SLC6A4

## D. Drug screening



# Early intervention? Development of a family-implemented program



## Treatment model:

- Begin: child's CI & family routines
- Goal: gradually broaden interests
  - tolerate delay, interruption of CI
  - try social contexts for CI
  - build new interests

Brian A. Boyd,<sup>1</sup> Cooper R. Woodard,<sup>2</sup> and James W. Bodfish<sup>3,4</sup>



**Feasibility of exposure response prevention to treat repetitive behaviors of children with autism and an intellectual disability: A brief report**

Autism  
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ORIGINAL PAPER

## Effects of a Family-Implemented Treatment on the Repetitive Behaviors of Children with Autism

Brian A. Boyd · Stephen G. McDonough ·  
Betty Rupp · Faraaz Khan · James W. Bodfish

## Family Implemented Treatment for Behavioral Inflexibility (FIT-BI)

Developed by:  
Brian Boyd  
Stephen McDonough  
Betty Rupp  
James Bodfish



A Treatment Manual to Guide Therapist & Parent Implementation



## Phenotype & measurement

*Lauren-Turner Brown-UNC, Allison Whitten - Vanderbilt*



## Peripheral biomarker (eye-tracking)

*Noah Sasson-UT Dallas, Jed Elison-U Minn, Kathryn Unruh- Vanderbilt*



## Reward circuitry (fMRI,fcMRI)

*Gabriel Dichter-UNC, Tony Richey-Virginia Tech*



## Mouse model (behavioral genetics, pharmacology)

*Sheryl Moy-UNC, Mark Lewis, U Fla, Robin Shafer-Vanderbilt*



## Early intervention

*Brian Boyd-UNC, Cooper Woodard-Groden Ctr*



## Adult ASD & Depression

*Kaite Gotham - Vanderbilt*

